REMARKS

Upon entry of the present amendment, claims 47-60 are pending in the application, claims 16, 39, 42-44, and 46 having been canceled by the present amendment. Claims 47 and 48 were amended to put them into condition for allowance as suggested by the Examiner. Claims 51-56 were amended to correct antecedent basis, and claims 58-60 were added to individually claim each member of the Markush group recited in independent claim 57.

No new matter has been added.

I. Claim Objection under 37 C.F.R. 1.75 (c)

Claims 42 and 43 were objected to for being of improper dependent form. This rejection can be withdrawn in view of the cancelation of claims 42 and 43.

II. Rejections under 35 U.S.C. § 112 (enablement)

Claim 42 and 43 were rejected for lack of enablement. On page 4, lines 23-29 of the Office Action, the Examiner states:

> It is noted that the hybridoma was deposited after the priority date of the instant application, and therefore a verified statement is required from a person in a position to corroborate that the deposited hybridoma is producing the monoclonal antibody FB50 as described in the specification as filed and is the same as that deposited in the depository, stating that the deposited hybridoma is producing the identical monoclonal antibody of FB50 as described in the specification and was in the applicant's possession at the time the application was filed is required.

Claims 42 and 43 have been canceled; however, Applicants note that claim 57 also recites monoclonal antibodies produced by hybridoma cell lines that were deposited with the ATCC under the terms of the Budapest Treaty. Accordingly, Applicants hereby submit a

Statement of Jack R. Wands Regarding Biological Culture Deposit indicating that the antibody-producing hybridoma cell lines described in the specification as filed are the same as those deposited with the ATCC and that the cell lines were in Applicants' possession at the time the patent application from which this divisional case claims priority was filed. Applicants believe that they are in full compliance with the requirements for biological material deposit practice in conjunction with a patent application. Withdrawal of this rejection is therefore respectfully requested.

Claims 39 and 57 were also rejected for lack of enablement. On pages 9-10, lines 22-28, of the Office Action, the Examiner states:

> the specification, while enabling for a method of inhibiting tumor growth in a mammal comprising the administration of an antibody conjugated to a chemotherapeutic agent which binds to an extracellular domain of HAAH, or the FB-50 antibody conjugated to a cytotoxic agent, does not reasonably provide enablement for a method of inhibiting tumor growth in a mammal comprising the administration of an antibody which binds the intracellular domain of HAAH....The specification does not teach the immunogen used to raise the 5C7, 19B or 86A antibodies, nor does it teach if said antibodies bind intracellular or extracellular epitopes. (emphasis added)

Claim 39 was canceled. Claim 57 requires monoclonal antibodies 5C7, 19B or 86A. With respect to the immunogen and binding specificity, the antibodies of the invention were made using the FOCUS hepatocellular carcinoma cell (HCC) line as the immunogen (see page 22, lines 9-23, and page 38, lines 9-19, of the specification). As described in the accompanying Declaration of Jack R. Wands, the monoclonal antibodies were further characterized by testing for binding to whole live cells and to formalin-fixed, paraffin-embedded tissue sections. Monoclonal antibodies 5C7, 86A, and 19B were found to recognize an epitope of HAAH expressed on the surface of malignant cells. These monoclonal antibodies bound to a soluble HAAH peptide containing the extracellular domain and lacking both the intracellular domain and transmembrane domain of HAAH, thereby confirming that the antibodies bind to an

epitope located in the extracellular domain of the protein. Applicants therefore request withdrawal of the rejection of claim 57.

III. Rejections under 35 U.S.C. § 112 (written description)

Claims 16, 44, 47-56 were rejected for lack of written description. Claims 16 and 44 were canceled. Claims 51-56 were amended to depend from claims 47 or 48.

In the paragraph spanning pages 5-6 of the Office Action, the Examiner made the following comments with respect to claims 47 and 48:

> Applicant states that the "allowability of claims 47 and 48 are acknowledged" however, claims 47 and 48 have been amended to recited "mutant comprising" over the former "mutant is" resulting in the rejection under 112, first above.....It is noted in the prior grounds of rejection that the claims are not limited to specific hydroxylation activity because the claims are drawn to the inhibition of "an enzymatic activity" rather than inhibition of hydroxylation (see page 11, lines 13 and 14 of section 13 of the previous Office Action). The prior version of claims 47 and 48 were not included under these grounds of rejection because the prior claims read on a mutant consisting of a substitution or a deletion at residue 679 and 690, respectively, and said mutants would inherently be confined to a genus characterized by both structure and hydroxylation.

Claims 47 and 48 have now been amended to require an HAAH mutant consisting of a substitution or deletion mutation at residue 679 or 690, respectively, in accordance with the Examiner's recommendations to put them into condition for allowance.

IV. Rejections under 35 U.S.C. § 103

Claims 16, 44, 46, 51, 53, and 54 were rejected for obviousness over Ullrich et al. and Lavaissiere et al. Claims 16, 44, and 46 were canceled. Claims 51, 53, and 54 were amended to depend from claims 47 or 48, which have been amended as indicated above to put them into condition for allowance. Accordingly, Applicants request withdrawal of this rejection.

Claims 42, 43, and 57 were rejected for obviousness over Schlom in view of Lavaissiere et al. On page 12, lines 15-18, of the Office Action, the Examiner states:

> It would have been *prima facie* obvious to one of ordinary skill in the art at the time the claimed invention was made to substitute the FB50 antibody as taught by Lavaissiere et al. in the general methods of inhibiting tumor growth in a mammal by the administration of antibodies and fragments thereof conjugated to chemotherapeutic agents or radio nuclides as taught by Schlom.

Claims 42 and 43 were canceled. Claim 57 requires monoclonal antibodies that are neither described or suggested by Schlom or Lavaissiere et al. Therefore, this rejection should be withdrawn.

CONCLUSION

Applicants submit that the application is in condition for allowance and such action is respectfully requested.

A petition for extension of time and a check in the amount of $950.00 is enclosed to cover the petition fee for a three month extension of time pursuant to 37 C.F.R. § 1.17(a)(3). The Commissioner is hereby authorized to charge any fees that may be due, or credit any overpayment of same, to Deposit Account No. 50-0311, Reference No. 21486-032 DIV2.

Should any questions or issues arise concerning the application, the Examiner is encouraged to contact the undersigned at the telephone number provided below.

Respectfully submitted,

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